IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicants:

Peter M. Glazer and Pamela A. Havre

Serial No.:

Continuation of 08/083,088

Express Mail Label

No.: El 709 418 853 US

Filed:

February 14, 2001

Date of Deposit: February 14, 2001

For:

CHEMICALLY MODIFIED OLIGONUCLEOTIDE FOR SITE-DIRECTED

MUTAGENESIS

Assistant Commissioner for Patents Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including four (4) pages of Form PTO-1449. The documents cited below were cited by or submitted to the Patent Office in Application Serial No. 08/083,088, filed June 25, 1993, to which the present application claims priority. Pursuant to 37 C.F.R. §1.98(d), Applicants are not enclosing copies of these publications. Copies will be provided upon request, however.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 01-2507.

Filed: February 14, 2001

INFORMATION DISCLOSURE STATEMENT

Foreign Documents

| <u>Number</u> | Publication Date | Patentee | Country |
|---------------|------------------|----------------------------|---------|
| 0 266 099 | 05-04-1988 | Johns Hopkins University | EP |
| 0 375 408 | 06-27-1990 | Baylor College of Medicine | EP |

Publications

BEAL, et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," *Science* 251:1360-1363 (1991).

BEAL, et al., "The Influence of Single Base Triplet Changes on the Stability of Pur-Pur-Pyr Triple Helix Determined by Affinity Cleaving," *Nuc. Acids Res.* 11:2773 (1992).

BLUME, et al., "Triple Helix Formation by Purine-Rich Oligonucleotides Targeted to the Human Dihydrofolate Reductase Promoter," *Nucleic Acids Rec.* 20:1777 (1992).

COONEY, "Site-Specific Oligonucleotide Binding Represses Transcription of the Human *c-myc* Gene in Vitro," *Science* 241:456 (1988).

DURLAND, "Binding of Triple Helix Forming Oligonucleotides to Sites in Gene Promoters," *Biochemistry* 30:9246 (1991).

DUVAL-VALENTIN, et al., "Specific Inhibition of Transcription by Triple Helix-Forming Oligonucleotides," *Proc. Natl. Acad. Sci. USA* 89:504 (1992).

FRANCOIS, "Sequence-Specific Recognition and Cleavage of Duplex DNA via Triple-Helix Formation by Oligonucleotides Covalently Linked to a Phenanthroline-Copper Chelate," *Proc. Natl. Acad. Sci. USA* 86:9702 (1989).

GASPARRO, et al., "Site-specific targeting of Psoralen Photoadducts with a Triple Helix-Forming Oligonucleotide: Characterization of Psoralen Monoadduct and Crosslink Formation," *Nucleic Acids Research*, 22(14):2845-2852 (1994).

GIOVANNANGELI, et al., "Oligodeoxynucleotide-directed photo-induced cross-linking of HIV proviral DNA via triple-helix formation," *Nucleic Acids Res.* 20:4275-4281 (1992).

GLAZER, et al., "Detection and Analysis of UV-induced Mutations in Mammalian Cell DNA Using A Phage Suttle Vector," *Proc. Natl. Acad. Sci.* 83:1041-1044 (1986).

GRIGORIEV, et al., "A Triple-Helix-Forming Oligonucleotide-Intercalator Conjugate Acts as a Transcriptional Repressor via Inhibition of NF $_kB$ Binding to Interleukin-2 Receptor α -Regulatory Sequence," *J. of Biological Chem.* 267:3389 (1992).

Filed: February 14, 2001

INFORMATION DISCLOSURE STATEMENT

GRIGORIEV, et al., "Inhibition of Gene Expression by Triple Helix-directed DNA Cross-linking at Specific Sites," *Proceedings of the National Academy of Sciences of USA*, 90(8):3501-3505 (1993)

HAVRE, et al., "Targed Mutagenesis of DNA Using Triple Helix-forming Oligonucleotides Linked to Psoralen," *Proc. Natl. Acad. Sci. USA*, 90(16):7879-7883 (1993).

ITO, et al., "Sequence-Specific DNA Purification by Triplex Affinity Capture," *Proc. Natl. Acad. Sci. USA* 89:495 (1992).

LIN, et al., "Use of EDTA Derivatization to Characterize Interactions Between Oligodeoxyribonucleoside Methylphosphonates and Nucleic Acids," *Biochemistry* 28:1054 (1989).

MAHER, et al., "Analysis of Promoter-Specific Repression by Triple Helical DNA Complexes in a Eukarvotic Cell-Free Transcription System," *Biochemistry* 31:70 (1992).

MAHER, et al., Science 245:725 (1989).

MERGNY, et al., "Sequence Specificity in Triple-Helix Formation: Experimental and Theoretical Studies of the Effect of Mismatches on Triplex Stability," *Biochemistry* 30:9791 (1991).

MIRABELLI, et al., "In Vitro and in vivo pharmacologic activities of antisense oligonucleotides," *Anticancer Design* 6:647-661 (1991).

MOSER, et al., "Sequence-Specific Cleavage of Double Helical DNA by Triple Helix Formation," *Science* 238:645 (1987).

ORSON, et al., "Oligonucleotide Inhibition of IL2Ra mRNA Transcription by Promoter Region Collinear Triplexed Formation in Lymphocytes," *Nucleic Acids Res.* 19:3435 (1991).

PEI, "Site Specific Cleavage of Duplex DNA by a Semisynthetic Nuclease via Triple-Helix Formation," *Proc. Natl. Acad. Sci. USA* 87:9858 (1990).

PERROUAULT, et al., "Sequence-Specific Artificial Photo-induced Endonuclease Based on Triple Helix-Forming Oligonucleotides," *Nature* 344:358 (1990).

POSTEL, et al., "Evidence that a Triple-Forming Oligodeoxyibonucleotide Binds to the *c-myc* Promoter in HeLa Cells, Thereby Reducing *c-myc* mRNA Levels," *Proc. Natl. Acad. Sci. USA* 88:8227 (1991).

POSVIC, et al., "Sequence-Specific lkylation of Double Helical DNA by Oligonucleotide Directed Triple-Helix Formation," J. Am. Chem. Soc. 112:9428 (1992).

Filed: February 14, 2001

INFORMATION DISCLOSURE STATEMENT

PRASEUTH, et al., "Sequence-Specific Binding and Photocrosslinking of α and β Oligodeoxynucleotides to the Major Groove of DNA via Triple-Helix Formation," *Proc. Natl. Acad. Sci. USA* 85:1349 (1988).

STROBEL, "Site-Specific Cleavage of Human Chromosone 4 Mediated by Triple-Helix Formation," *Science* 254:1639 (1991).

TAKASUGI, et al., "Sequence-specific Photo-Induced Cross-Linking of the Two Strands of Double-Helical DNA by a Psoralen Covalently Linked to a Triple Helix Forming Oligonucleotide," *Proceedings of the National Academy of Sciences of USA* 88(13):5602-5606 (1991).

UHLMAN, et al., "Antisense Oligonucleotides: A New Therapeutic Principle," *Chem. Reviews* 90(4):544-584 (1990).

WOOD, et al., "The Effect of Volume and Temperature on the Energy and Entropy of Pure Liquids," *J. Am. Chem. Soc.* 79:2023 (1957).

YOUNG, "Triple Helix Formation Inhibits Transcription Elongation in vitro," Proc. Natl. Sci. USA 88:10023 (1991).

Filed: February 14, 2001

INFORMATION DISCLOSURE STATEMENT

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,

Robert A. Hodges Reg. No. 41,074

Dated: February 14, 2001

ARNALL GOLDEN & GREGORY, LLP 2800 One Atlantic Center 1201 W. Peachtree Street Atlanta, Georgia 30309-3450 (404) 873-8794 (404) 873-8795 (fax) Sheet

YU 109 CON



of

4

Examiner Name

Attorney Docket Number

| U.S. PATENT DOCUMENTS | | | | | | | | |
|-----------------------|--------------|--------|----------|-----------------------------|------|---|-----------------------------------|--|
| | Cite No.¹ | | US Pater | nt Docu | ment | Name of Patentee or Applicant of Cited Document | Date of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number | | Code ² (nown) | | | | |
| - | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | - | | | | | | | |
| | | | | | | | | |

| | | | | | FOREIGN PATENT DOCUMEN | TS | | | | | |
|---|--------------|----------|---------------------|--------------------------------------|----------------------------|------------|--|--|--|---|----------------|
| | Cite No.¹ | | | | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| ! | | Office.3 | Number ⁴ | Kind Code ⁵ (if known) | | | | | | | |
| | | EP | 0 266 099 | | Johns Hopkins University | 05-04-1988 | | | | | |
| | | EP | 0 375 408 | | Baylor College of Medicine | 06-27-1990 | | - | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | <u>. j</u> | | | |

| Examine | Date | |
|-----------|------------|--|
| Signature | Considered | |

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ³ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Sheet

2

of

YU 109 CON

| Substitute for form 1449A/PTO | | Complete if Known | |
|--|----------------------|----------------------------|--|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | Application Number | Continuation of 08/083,088 | |
| (use as many shocks as hoodstary) | Filing Date | February 14, 2001 | |
| | First Named Inventor | Peter M. Glazer | |
| | Group Art Unit | | |
| | Examiner Name | | |

Attorney Docket Number

4

| | | OTHER ART NON PATENT LITERATURE DOCUMENTS | T ² |
|-------------------------|--------------|--|----------------|
| Examiner's Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | |
| | | BEAL, et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," Science 251:1360-1363 (1991). | |
| | | BEAL, et al., "The Influence of Single Base Triplet Changes on the Stability of Pur-Pur-Pyr Triple Helix Determined by Affinity Cleaving," <i>Nuc. Acids Res.</i> 11:2773 (1992). | |
| | , | BLUME, et al., "Triple Helix Formation by Purine-Rich Oligonucleotides Targeted to the Human Dihydrofolate Reductase Promoter," <i>Nucleic Acids Rec.</i> 20:1777 (1992). | |
| | | COONEY, "Site-Specific Oligonucleotide Binding Represses Transcription of the Human <i>c-myc</i> Gene in Vitro," <i>Science</i> 241:456 (1988). | |
| | | DURLAND, "Binding of Triple Helix Forming Oligonucleotides to Sites in Gene Promoters," <i>Biochemistry</i> 30:9246 (1991). | |
| | | DUVAL-VALENTIN, et al., "Specific Inhibition of Transcription by Triple Helix-Forming Oligonucleotides," <i>Proc. Natl. Acad. Sci. USA</i> 89:504 (1992). | |
| | | FRANCOIS, "Sequence-Specific Recognition and Cleavage of Duplex DNA via Triple-Helix Formation by Oligonucleotides Covalently Linked to a Phenanthroline-Copper Chelate," <i>Proc. Natl. Acad. Sci. USA</i> 86:9702 (1989). | |
| | _ | GASPARRO, et al., "Site-specific targeting of Psoralen Photoadducts with a Triple Helix-Forming Oligonucleotide: Characterization of Psoralen Monoadduct and Crosslink Formation," <i>Nucleic Acids Research</i> , 22(14):2845-2852 (1994). | |
| | | GIOVANNANGELI, et al., "Oligodeoxynucleotide-directed photo-induced cross-linking of HIV proviral DNA via triple-helix formation," <i>Nucleic Acids Res.</i> 20:4275-4281 (1992). | |
| | | GLAZER, et al., "Detection and Analysis of UV-induced Mutations in Mammalian Cell DNA Using A Phage Suttle Vector," <i>Proc. Natl. Acad. Sci.</i> 83:1041-1044 (1986). | |

| Examiner's | Date |
|------------|------------|
| Signature | Considered |

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

| | PΤ | 0/58/0 | BA (1 | 0-9 |
|--|------|--------|-------|-----|
| Approved for use through 10/31/ | 199. | OMB 0 | 651- | 003 |
| Partent and Trademark Office: U.S. DEPARTI | MEN | T OF C | MMC | ERC |

| nder the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of info | ormation unless it contains a valid OMB control number | | | | |
|--|--|----------------------------|--|--|--|
| Substitute for form 1449A/PTO | Co | Complete if Known | | | |
| INFORMATION DISCLOSUR STATEMENT BY APPLICAN (use as many sheets as necessary) | | Continuation of 08/083,088 | | | |
| (455 45 11141) (11141) | Filing Date | February 14, 2001 | | | |
| | First Named Inventor | Peter M. Glazer | | | |
| | Group Art Unit | | | | |
| | Examiner Name | | | | |
| hoot 3 of 4 | Attorney Docket Number | YU 109 CON | | | |

| | | OTHER ART NON PATENT LITERATURE DOCUMENTS | |
|------------------------|--------------|--|---|
| xaminer's Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T |
| | | GRIGORIEV, et al., "A Triple-Helix-Forming Oligonucleotide-Intercalator Conjugate Acts as a Transcriptional Repressor via Inhibition of NF _k B Binding to Interleukin-2 Receptor α-Regulatory Sequence," <i>J. of Biological Chem.</i> 267:3389 | |
| | | GRIGORIEV, et al., "Inhibition of Gene Expression by Triple Helix-directed DNA Cross-linking at Specific Sites," Proceedings of the National Academy of Sciences of USA, 90(8):3501-3505 (1993) | |
| | | HAVRE, et al., "Targed Mutagenesis of DNA Using Triple Helix-forming Oligonucleotides Linked to Psoralen," <i>Proc. Natl. Acad. Sci. USA</i> , 90(16):7879-7883 (1993). | |
| | | ITO, et al., "Sequence-Specific DNA Purification by Triplex Affinity Capture," <i>Proc. Natl. Acad. Sci. USA</i> 89:495 (1992). | |
| | | LIN, et al., "Use of EDTA Derivatization to Characterize Interactions Between Oligodeoxyribonucleoside Methylphosphonates and Nucleic Acids," <i>Biochemistry</i> 28:1054 (1989). | |
| | | MAHER, et al., "Analysis of Promoter-Specific Repression by Triple Helical DNA Complexes in a Eukarvotic Cell-Free Transcription System," <i>Biochemistry</i> 31:70 (1992). | |
| | | MAHER, et al., Science 245:725 (1989). | |
| | | MERGNY, et al., "Sequence Specificity in Triple-Helix Formation: Experimental and Theoretical Studies of the Effect of Mismatches on Triplex Stability," <i>Biochemistry</i> 30:9791 (1991). | |
| | | MIRABELLI, et al., "In Vitro and in vivo pharmacologic activities of antisense oligonucleotides," <i>Anticancer Design</i> 6:647-661 (1991). | |
| | - | MOSER, et al., "Sequence-Specific Cleavage of Double Helical DNA by Triple Helix Formation," Science 238:645 (1987). | |

| Examiner's | Date |
|------------|------------|
| Signature | Considered |
| | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

| | Substitute for | | OA/PTO | Complete if Known | | | |
|-------|----------------|------------|--|------------------------|----------------------------|--|--|
| | STATE | MENT | N DISCLOSURE BY APPLICANT eets as necessary) | Application Number | Continuation of 08/083,088 | | |
| | (use a | 15 many 50 | sets as riccessury/ | Filing Date | February 14, 2001 | | |
| | | | | First Named Inventor | Peter M. Glazer | | |
| | | | | Group Art Unit | | | |
| | | | | Examiner Name | | | |
| Sheet | 4 | of | 4 | Attorney Docket Number | YU 109 CON | | |

| | | OTHER ART NON PATENT LITERATURE DOCUMENTS |
|------------------------|--------------------------|--|
| xaminer's Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), mublisher, city and/or country where published |
| | | ORSON, et al., "Oligonucleotide Inhibition of IL2Ra mRNA Transcription by Promoter Region Collinear Triplexed Formation in Lymphocytes," <i>Nucleic Acids Res.</i> 19:3435 (1991). |
| | | PEI, "Site Specific Cleavage of Duplex DNA by a Semisynthetic Nuclease via Triple-Helix Formation," <i>Proc. Natl. Acad. Sci. USA</i> 87:9858 (1990). |
| | | PERROUAULT, et al., "Sequence-Specific Artificial Photo-induced Endonuclease Based on Triple Helix-Forming Oligonucleotides," <i>Nature</i> 344:358 (1990). |
| | | POSTEL, et al., "Evidence that a Triple-Forming Oligodeoxyibonucleotide Binds to the <i>c-myc</i> Promoter in HeLa Cells, Thereby Reducing <i>c-myc</i> mRNA Levels," <i>Proc. Natl. Acad. Sci. USA</i> 88:8227 (1991). |
| , | | POSVIC, et al., "Sequence-Specific Ikylation of Double Helical DNA by Oligonucleotide Directed Triple-Helix Formation," J. Am. Chem. Soc. 112:9428 (1992). |
| | | PRASEUTH, et al., "Sequence-Specific Binding and Photocrosslinking of α and β Oligodeoxynucleotides to the Major Groove of DNA via Triple-Helix Formation," <i>Proc. Natl. Acad. Sci. USA</i> 85:1349 (1988). |
| | | STROBEL, "Site-Specific Cleavage of Human Chromosone 4 Mediated by Triple-Helix Formation," Science 254:1639 (1991). |
| | | TAKASUGI, et al., "Sequence-specific Photo-Induced Cross-Linking of the Two Strands of Double-Helical DNA by a Psoralen Covalently Linked to a Triple Helix Forming Oligonucleotide," <i>Proceedings of the National Academy of Sciences of USA</i> 88(13):5602-5606 (1991). |
| | | UHLMAN, et al., "Antisense Oligonucleotides: A New Therapeutic Principle," Chem. Reviews 90(4):544-584 (1990). |
| | | WOOD, et al., "The Effect of Volume and Temperature on the Energy and Entropy of Pure Liquids," J. Am. Chem. Soc. 79:2023 (1957). |
| | - | YOUNG, "Triple Helix Formation Inhibits Transcription Elongation in vitro," Proc. Natl. Sci. USA 88:10023 (1991). |

| Examiner's Date Signature Considered | | | |
|---------------------------------------|------------|------------|-----|
| I I I I I I I I I I I I I I I I I I I | Evaminar's | Date | |
| Signature | Examine 5 | Considered | i i |
| | Signature | Considered | |

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Filed: February 14, 2001

INFORMATION DISCLOSURE STATEMENT

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this INFORMATION DISCLOSURE STATEMENT and any documents referred to as attached therein are being deposited with the United States Postal Service on this date, February 14, 2001, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Mailing Label Number EL 709 418 853 US, addressed to BOX PATENT APPLICATION, Assistant Commissioner for Patents, Washington, D.C. 20231.

Teresa R Spratt

Date: February 14, 2001